

## **General Disclaimer**

### **One or more of the Following Statements may affect this Document**

- This document has been reproduced from the best copy furnished by the organizational source. It is being released in the interest of making available as much information as possible.
- This document may contain data, which exceeds the sheet parameters. It was furnished in this condition by the organizational source and is the best copy available.
- This document may contain tone-on-tone or color graphs, charts and/or pictures, which have been reproduced in black and white.
- This document is paginated as submitted by the original source.
- Portions of this document are not fully legible due to the historical nature of some of the material. However, it is the best reproduction available from the original submission.

MORPHOLOGICAL AND FUNCTIONAL MANIFESTATIONS  
OF RAT ADRENAL-CORTEX RESPONSE TO SODIUM BROMIDE  
ADMINISTRATION UNDER HYPODYNAMIC STRESS

L. T. Kirichek, V. I. Zholudeva

Translation of: "Morfofunktsional'nyye proyavleniya  
reaktsii kory nadpochechnikov krys na vvedeniye bro-  
mida natriya v usloviyakh gipodinamicheskogo stressa,"  
Farmakologiya i Toksikologiya, Vol. 38, No. 6, Nov.-  
Dec. 1975, pp. 703-706.

(NASA-TM-75953) MORPHOLOGICAL AND FUNCTIONAL  
MANIFESTATIONS OF RAT ADRENAL-CORTEX  
RESPONSE TO SODIUM BROMIDE ADMINISTRATION  
UNDER HYPODYNAMIC STRESS (National  
Aeronautics and Space Administration) 12 p 63/51

N80-16719

Unclas  
46921



NATIONAL AERONAUTICS AND SPACE ADMINISTRATION  
WASHINGTON, D.C. 20546  
NOVEMBER 1979

**MORPHOLOGICAL AND FUNCTIONAL MANIFESTATIONS OF  
RAT ADRENAL CORTEX RESPONSE TO SODIUM BROMIDE  
ADMINISTRATION UNDER HYPODYNAMIC STRESS**

by

L. T. Kirichek and V. I. Zholudeva  
Department of Pharmacology (Head: Professor N. S.  
Kharchenko) and Department of Pathological Anatomy  
(Head: Doctor of Medical Sciences A. F. Yakovtsova)  
of the Khar'kov Medical Institute

Functional and morphological manifestations of adrenal cortex response to hypodynamia (2-hour immobilization on an operating table) under the influence of bromine preparations were studied in experiments on 132 rats. The sodium bromide was administered intraperitoneally in 100, 250 and 500 mg/kg doses once and repeatedly during 10 days. The adrenal gland was analyzed functionally by ascorbic acid and cholesterol content, and morphologically by staining with hematoxylin-eosin and Sudans for lipid detection at freezing. Results are displayed in two tables and in microphotographs. They are summarized as follows: the bromine weakens the functional state of the adrenal cortex in intact rats, causing changes similar to those under stress. During immobilization combined with preliminary bromine administration, a less pronounced stress reaction is noticeable.

It is known that the processes of self-regulation can be the object of pharmacological influence to the same measure as the specific functions of individual systems and organs (N. V. Lazarev, 1962; I. I. Brekhman and O. I. Kirillov, 1965; O. I.

/703\*

---

Numbers in margin indicate pagination in original foreign text.

Kirillov, 1966; V. M. Vinogradov, 1973; Ye. A. Mukhin and E. B. Keptya, 1973). This acquires especial importance in stress when the activity of the adaptive mechanisms is intensified (G. Sel'ye, 1960; P. K. Anokhin, 1965; P. D. Gorizontov and T. N. Protasova, 1968). The effects of the neurotropic resources of damping type of action must be the most adequate to this state.

Previously we demonstrated that in the central action of bromine a definite role is played by its effect on the limbic-reticular structure of the brain that refers to the processes of self-regulation (L. T. Kirichek and P. V. Voloshin, 1973). This was reflected in the reduction in endurance of intact animals to the effect of such external factors as overheating, overcooling, physical load and rotation, as well as in the attenuation in the pronounced nature of stress in animals exposed to stretching (L. T. Kirichek, 1971).

The task of this work included study of the functional and morphological manifestations of the adrenal cortex reaction under the influence of bromine preparations in animals under immobilization, since hypodynamia is one of the main problems of the pathological physiology of modern extreme states (P. P. Golikov, M. A. Medvedev, 1969; K. M. Smirnov, 1970; B. M. Fedorov et al., 1973).

### Methods of Study

Experiments were made on 132 albino rats weighing 100-150 g. Sodium bromide was administered intragastrically in the form of 1-5 and 10% aqueous solution in doses that acted on the therapeutic level in the animals (I. P. Zapadnyuk et al., 1974). The substance was administered in different doses (100, 250, 500 mg/kg) once or repeatedly for 10 days; studies were made in different times (within 1, 2, 3 and 4 h after single administration and at the end of the 10-day experiment) on intact animals (I series)

and rats exposed to two-hour immobilization on an operating table (II series). Animals who received a physiological solution of sodium chloride under analogous conditions served as the control.

The functional state of the adrenal glands was analyzed according to the content in them of ascorbic acid by the Birch et al. method (1933) and cholesterol by the Engel'gardt method (N. N. Pushkina, 1963). In addition to this a morphological method was used to study the adrenal glands with staining by hematoxylin-eosin, picrofuchsin (van Gieson), as well as Sudan III and Black Sudan B to detect lipids during freezing.

### Results

As is apparent from table 1, the administration of bromine to intact animals weakened the functional state of the adrenal cortex which was indicated by an increase in the content in them of ascorbic acid and reduction in the cholesterol level.

Table 1

/704

EFFECT OF SODIUM BROMIDE ON CONTENT OF ASCORBIC ACID AND CHOLESTEROL IN ADRENAL GLANDS OF INTACT RATS (M $\pm$  m)

Index	Control	Administration of sodium bromide				
		single (dose in mg/kg)			repeated 250 mg/kg, 10 days	
		100	250	500		
Ascorbic acid(in mg%) D	258,8 $\pm$ 9,2	332,7 $\pm$ 34,3 <0,05	277,5 $\pm$ 13,9 >0,05	338,7 $\pm$ 14,1 <0,05	343,0 $\pm$ 18,8 <0,05	
Cholesterol(in mg%) D	1812 $\pm$ 310	1111 $\pm$ 78 <0,05	1072 $\pm$ 83 <0,05	814 $\pm$ 75 <0,05	1614 $\pm$ 126 <0,05	

In the morphological tissue study of the adrenal cortex in the first series in all periods of observation no significant differences were found between the control rats and the rats who had received a single sodium bromide administration in doses of 100 and 250 mg/kg. An increase in the dose to 500 mg/kg in

TABLE 2

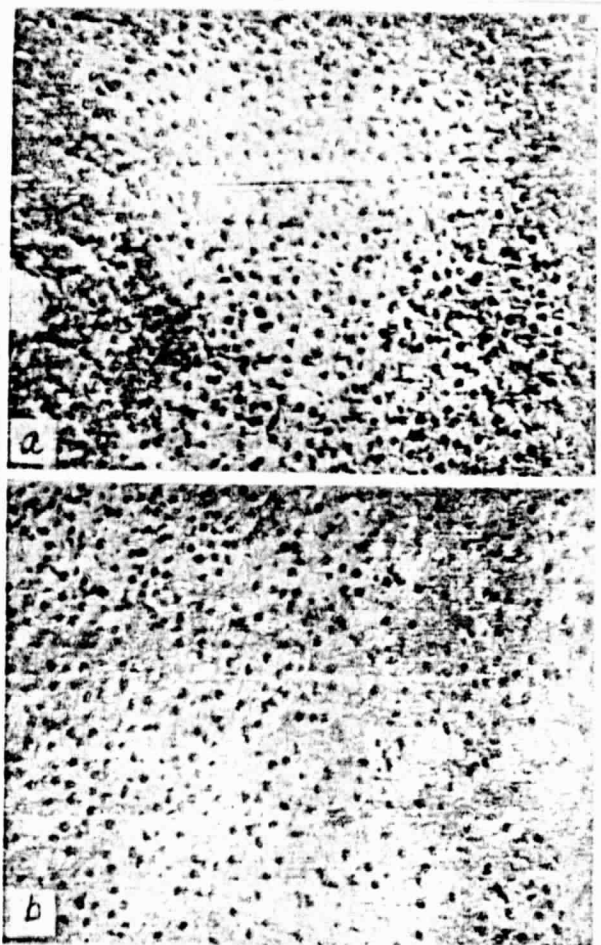
EFFECT OF SODIUM BROMIDE ON CONTENT OF ASCORBIC ACID AND CHOLESTEROL IN ADRENAL GLANDS OF RATS EXPOSED TO IMMOBILIZATION (M+m)

Index	Control	Stress	Administration of sodium bromide + stress			
			single administration (dose in mg/kg)			repeated administration (250 mg/kg, 10 days)
			100	250	500	
Ascorbic acid (in mg%) D	258,8±9,2	324,9±12,1 <0,05	291,7±11,1 >0,05	243,6±14,2 <0,05	214±22,9 <0,05	252,6±19,6 >0,05
Cholesterol (in mg%) D	1812±310	1162±18,1 >0,05	969±156 <0,05	796±68 <0,05	786±50 <0,05	1897±158 <0,05

these conditions led to the appearance in the rat adrenal cortex of pronounced vascular (plethora of vessels in swollen reticular zone, fine-grained vacuolization of cytoplasm of cells in reticular zone, edema of its connective tissue stroma), as well as dystrophic (appearance of small-cellular formation of cytoplasm of cells in fascicular zone and protein eosinophil mass in the sinusoids) changes (see figure). This was accompanied by a reduction in the amount of lipids in the adrenal cortex cells which also reflected the attenuation in their functions, although certain signs of their compensation were also revealed (expansion of the fascicular zone). The described phenomena increased from the first to fourth hour after single administration of bromide and were more pronounced in the cases of repeated administration of the preparation.

At the end of the 10-day experiment a more pronounced suppression was noted in the functional state of the adrenal cortex: a considerably greater loss of fat and lipids was noted, excess content in the fascicular and reticular zones of the adrenal cortex of so-called dark cells, which indicated the state of prolonged impoverishment.





State of Adrenal Cortex in Rats Normally (a) and with Single Administration of Sodium Bromide in Dose 500 mg/kg (b). Staining with hematoxylin-eosin. Mag. 200 x.

Two-hour immobilization of the rats resulted in attenuation of the functional state of the adrenal cortex. As is apparent from table 2, here the quantity of ascorbic acid in the adrenal glands was increased, while cholesterol and its esters was reduced. The morphological picture of the adrenal cortex still reflected its active state: the glomerular zone and the outer layer of the fascicular zone consisted of light cells with fine-grained cytoplasm filled with lipid droplets. /705

The single and repeated administration of sodium bromide that preceded the hypodynamic stress restored the content of ascorbic acid in the adrenal cortex of rats to the initial. The content of cholesterol in the adrenal glands with single administration of sodium bromide progressively dropped, and with repeated administration reached the initial figures.

Morphologically under these conditions disruptions were found in the form of edema of the capsule, fascicular zone, stroma of the cerebral substance, swelling and vacuolization of individual cells of it, plasmorrhagia more pronounced than in the intact animals. In addition, in the adrenal cortex pronounced compensatory phenomena dominated: dilatation of the glomerular zone due to the direct and indirect division of cells, presence of foci of hypertrophied and hyperplastic cells of the glomerular and fascicular zone with penetration of part of them into medulla. In the experiments with repeated administration of sodium bromide in the cells of the fascicular zone, especially in its outer part a large number of fine- and large-dispersed lipids were noted.

Thus, as the data showed of the functional and morphological study the activity of the adrenal cortex in intact rats under the influence of sodium bromide is weakened. An analogous effect is produced by the state of hypodynamic stress. Immobilization on the background of sodium bromide administration, evidently, is endured by the animals more easily. Such an effect was noted by G. Neshev (1970) with aminazine, which, in the author's opinion, has a positive effect on the development of stress, since the so-called repeated aggression is inherent to it that is governed by the ability of the preparation to produce in intact animals shifts that are characteristic for the stress reaction.

/706



## Conclusions

1. Sodium bromide with single intragastric administration in a dose of 500 mg/kg and repeated administration for 10 days in a dose of 250 mg/kg weakens the functional state of the adrenal cortex in intact rats.

2. Preliminary administration of sodium bromide in the studied intervals of doses and periods reduces the manifestation in rats of the stress reaction induced by 2-hour immobilization.

## References

- Anokhin, P. K. in Refleksy golovnogo mozga [Reflexes of the Brain] Moscow, 1965, 297-311.
- Brekhman, I. I. and Kirillov, O. I. in Materialy 22-y nauchnoy sessii Khabarovskogo med. in-ta ["Materials of 22nd Scientific Session of Khabarovsk Medical Institute"], Khabarovsk, 1965, 212-213.
- Vinogradov, V. M. in Povysheniye rezistentnosti organizma k ekstremal'nykh vozdeystviyam ["Increase in Resistance of Organism to Extreme Effects"], Kishinev, 1973, 105-127.
- Golikov, P. P. and Medvedev, M. A. in Materialy nauchnoy sessii Vsesoyuznogo nauch.-issled. in-ta fizkul'tury za 1967 ["Materials of Scientific Session of All-Union Sci.Res. Institute of Physical Culture for 1967"], 1969, p. 370-371.
- Gorizontov, P. D. and Protasova, T. N. Rol' AKTG i kortikosteroidov v patologii ["Role of ACTH and Corticosteroids in Pathology"], Moscow, 1968, 98-122.
- Zapadnyuk, I. P.; Zapadnyuk, V. I. and Zakhariya, Ye. A. Laboratornyye zhivotnyye, ikh razvedeniye, soderzhaniye i ispol'zovaniye v eksperimente ["Laboratory Animals, Their Breeding, Maintenance and Use in Experiment"], Kiev, 1974, 285.
- Kirillov, O. I. Opyt farmakologicheskoy regulyatsii stressa ["Experimental Pharmacological Regulation of Stress"], Vladivostok, 1966, 6-25.
- Kirichuk, L. T. Sovremennyye problemy farmakologii ["Current Problems in Pharmacology"], Kiev, 1971, 114-115.

- Kirichek, L. T. and Voloshin, P. V. Materialy 2-go s"yezda farmakologov Ukrainskoy SSR ["Materials of Second Congress of Pharmacologists of the Ukrainian SSR"], 1973, 97-98.
- Lazarev, N. V. Simpoziumy po eleuterokokku i zhen'shenyu ["Symposiums on Eleutherococcus and Ginseng"], Vladivostok, 1962, 7-10.
- Mukhin, Ye. A. and Keptya, E. B. Povisheniye rezistentnosti organizma k ekstremal'ny'm vozdeystviyam ["Increase in Resistance of Organism to Extreme Factors"], Kishinev, 1973, 5-20.
- Neshev, G. Pat. fiziol., 1970, No. 5, 42-46.
- Pushkina, N. N. Biokhimicheskiye metody issledovaniya ["Biochemical methods of Research"], Moscow, Meditsina, 1963, 114-117.
- Sel'ye, G. Ocherki ob adaptatsionnom sindrome ["Essays on the Adaptation Syndrome"], Moscow, 1960.
- Smirnov, K. M., Gig. i san., No. 2 (1970), p. 74-78.
- Fedorov, B. M., Krotov, V. P., and Zhuravleva, Ye. N. Pat. fiziol. No. 6 (1973), 27-31.
- Birch, T. K., Harris, L. J. and Roy, S. N. Biochem. J., Vol. 27, (1933), 590-594.

Copyright Holder: "Farmakologiya i toksikologiya", 1975